



DOCKET NO.: ADOL-0712

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Roland E. Dolle

Confirmation No.: Not Yet Assigned

Application No.: 10/798,664

Group Art Unit: Not Yet Assigned

Filing Date: March 11, 2004

Examiner: Not Yet Assigned

For: **SUBSTITUTED PIPERIDINE COMPOUNDS AND METHODS OF THEIR USE**

DATE OF DEPOSIT:

*April 16, 2004*

I HEREBY CERTIFY THAT THIS PAPER IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE AS FIRST CLASS MAIL, POSTAGE PREPAID, ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO THE UNITED STATES PATENT AND TRADEMARK OFFICE, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450.

*Elizabeth A. McLoud*

TYPED NAME: Elizabeth A. McLoud

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

INFORMATION DISCLOSURE STATEMENT

Pursuant to 37 CFR § 1.56 and in accordance with 37 CFR §§ 1.97-1.98, information relating to the above-identified application is hereby disclosed. Inclusion of information in this statement is not to be construed as an admission that this information is material as that term is defined in 37 CFR § 1.56(b).



In accordance with § 1.97(b), since this Information Disclosure Statement is being filed either within three months of the filing date of the above-identified application, within three months of the date of entry into the national stage of

the above identified application as set forth in § 1.491, before the mailing date of a first Office Action on the merits of the above-identified application, or before the mailing date of a first Office Action after the filing of request for continued examination under § 1.114, no additional fee is required.

- ☐ In accordance with § 1.129(a), this Information Disclosure Statement is being filed in connection with ☐ the first or ☐ second After Final Submission, therefore:

☐ Certification in Accordance with § 1.97(e) is attached; or

☐ The fee of **\$180.00** as set forth in § 1.17(p) is attached.

- ☐ In accordance with § 1.97(c), this Information Disclosure Statement is being filed after the period set forth in § 1.97(b) above but before the mailing date of either a Final Action under § 1.113 or a Notice of Allowance under § 1.311, or before an action that otherwise closes prosecution in the application, therefore:

☐ Certification in Accordance with § 1.97(e) is attached;

or

☐ The fee of **\$180.00** as set forth in § 1.17(p) is attached.

- ☐ In accordance with § 1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under § 1.113 or a Notice of Allowance under § 1.311 but before, or simultaneously with, the payment of the Issue Fee, therefore included are: Certification in Accordance with § 1.97(e); and the submission fee of **\$180.00** as set forth in § 1.17(p).

- ☐ Copies of each of the references listed on the attached Form PTO-1449 are enclosed herewith.

- ☒ Copies of references listed on the attached Form PTO-1449 are enclosed herewith
- ☒ Copies of references listed on the attached Form PTO 1449 are not required to be submitted pursuant to the June 30, 2003 recent revisions to 37 CFR § 1.98(a)(2)(i).


## EXCEPT THAT:

- ☒ In view of the voluminous nature of references 5, 10, 20 and 22, and the likelihood that these references are available to the Examiner, copies are not enclosed herewith.
- ☐ In accordance with § 1.98(d), copies of the following references listed on the attached Form PTO-1449 are not enclosed herewith because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application(s) for which a claim for priority under 35 U.S.C. § 120 have been made in the instant application:
- ☐ Copies of references [list as appropriate] listed on the attached Form PTO-1449 were previously cited by or submitted to the Patent and Trademark Office in prior Application No. \_\_\_\_\_, filed \_\_\_\_\_.

Please charge any deficiency or credit any overpayment to Deposit Account No. 23-3050. This form is submitted in duplicate.

- ☐ The relevance of those listed references which are not in the English language is as follows:
- ☒ There are no listed references which are not in the English language.

Date: April 16, 2004

  
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<b>Form PTO-1449 Modified</b>  List of Patent and Publications Cited by Applicant (Use several sheets if necessary)  U.S. Department of Commerce Patent and Trademark Office		Docket No. ADOL-0712	Application No. 10/798,664
		Applicant Roland E. Dolle	
		Filing Date March 11, 2004	Group Not Yet Assigned
		Confirmation No. Not Yet Assigned	
<b>OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)</b>			
	1	Bagnol, D., et al., "Changes in enkephalin immunoreactivity of sympathetic ganglia and digestive tract of the cat after splanchnic nerve ligation," <i>Regul. Peptides</i> , <b>1993</b> , 47, 259-273	
	2	Bagnol, D., et al., "Cellular localization and distribution of the cloned mu and kappa opioid receptors in rat gastrointestinal tract," <i>Neuroscience</i> , <b>1997</b> , 81(2), 579-591	
	3	Bhargava, H.N., et al., "Effect of nitric oxide synthase inhibition on tolerance to the analgesic action of D-Pen <sup>2</sup> , D-Pen <sup>5</sup> enkephalin and morphine in the mouse," <i>Neuropeptides</i> , <b>1996</b> , 30(3), 219-223	
	4	Bilsky, E.J., "Effects of naloxone and D-phe-cys-tyr-D-trp-arg-thr-pen-thr-NH <sub>2</sub> and the protein kinase inhibitors H7 and H8 on acute morphine dependence and antinociceptive tolerance in mice," <i>J. Pharmacol. Exp. Ther.</i> , <b>1996</b> , 277, 484-490	
*	5	Buschmann, H., et al., Verlag GMbH & Co. KgaA, Weinheim, <b>2002</b>	
	6	Dorland's Illustrated Medical Dictionary, 27 <sup>th</sup> Ed., W.B. Saunders Co., Phila., PA, <b>1988</b> , page 816	
	7	Dorland's Illustrated Medical Dictionary, 27 <sup>th</sup> Ed., W.B. Saunders Co., Phila., PA, <b>1988</b> , page 375	
	8	Dourish, C.T., et al., "Enhancement of morphine analgesia and prevention of morphine tolerance in the rat by the cholecystokinin antagonist L-364, 718," <i>Eur. J. Pharmacol.</i> , <b>1988</b> , 147, 469-472	
	9	Drewes, S.E., et al., "Synthesis, resolution and assignment of absolute configuration of 2-( $\alpha$ -hydroxy)aryl acrylate esters," <i>Tetrah. Asymmetry</i> , <b>1992</b> , 3(2), 255-260	
*	10	Greene, T.W., et al., Protective Groups in Organic Synthesis, 3 <sup>rd</sup> Ed., Wiley & Sons, <b>1991</b>	
<b>EXAMINER</b>		<b>DATE CONSIDERED</b>	

\* A copy of these references will not be forwarded to the U.S. Patent and Trademark Office since they are believed to be too voluminous and easily obtainable by the Examiner.

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	11	Jain, K.K., "A guide to drug evaluation for chronic pain," <i>Emerging Drugs</i> , 2000, 5(2), 241-257	
	12	Koch, T.R., et al., "Inhibitory neuropeptides and intrinsic inhibitory innervation of descending human colon," <i>Digestive Diseases &amp; Sciences</i> , 1991, 36(6), 712-718	
	13	Kreek, M.-J., et al., "Naloxone, a specific opioid antagonist, reverses chronic idiopathic constipation," <i>J. Lancet</i> , 1983, 261-262	
	14	Livingston, E.H., et al., "Postoperative ileus," <i>Digestive Diseases and Sciences</i> , 1990, 35(1), 121-132	
	15	Mack, D.J., "Paralytic ileus: response to naloxone," <i>Br. J. Surg.</i> , 1989, 76(10), page 1101	
	16	Mao, M.J., et al., "Oral administration of dextromethorphan prevents the development of morphine tolerance and dependence in rats," <i>Pain</i> , 1996, 67, 361-368	
	17	Nichols, M.L., et al., "Enhancement of the antiallodynic and antinociceptive efficacy of spinal morphine by antisera to dynorphin A (1-13) or MK-801 in a nerve-ligation model of peripheral neuropathy," <i>Pain</i> , 1997, 69, 317-322	
	18	Perlmutter, P., et al., "A simple route to $\alpha$ -substituted- $\beta$ -amino ester precursors of carbapenem antibiotics," <i>J. Org. Chem.</i> , 1995, 60, 6515-6522	
	19	Perlmutter, P., et al., "Diastereoselection in the nucleophilic conjugate addition of amines to 2-hydroxyalkylpropenoates," <i>Tetrah. Lett.</i> , 1988, 29(8), 949-952	
*	20	Physician's Desk Reference, 1999	
<b>EXAMINER</b>			<b>DATE CONSIDERED</b>

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	21	Reisine, T., et al., "Opioid analgesics and antagonists," <i>Goodman &amp; Gilman's The Pharmacological Basis of Therapeutics</i> , 9 <sup>th</sup> Ed., 1996, Chapter 23, 521-555	
*	22	Remington's Pharmaceutical Sciences, Mack Pub. Co., Easton, PA, 1980	
.	23	Resnick, J., et al., "Delayed gastric emptying and postoperative Ileus after nongastric abdominal surgery: Part I," <i>Am. J. of Gastroenterology</i> , 1997, 92(5), 751-762	
.	24	Resnick, J., et al., "Delayed gastric emptying and postoperative ileus after nongastric abdominal surgery: Part II," <i>Am. J. of Gastroenterology</i> , 1997, 92(6), 934-940	
	25	Schang, J.C., et al., "Beneficial effects of naloxone in a patient with intestinal pseudoobstruction," <i>Am. J. Gastroenterol</i> , 1985, 80(6), 407-411	
	26	Schuller, A.G.P., et al., "M6G, but not morphine, inhibits GI transit in MU opioid receptor deficient mice," Abstract No. 210.7, <i>Society of Neurosc.</i> , 1998, 24, page 524	
	27	Shaw, W.N., et al., "Effect of phenylpiperidine opioid antagonists on food consumption and weight gain of the obese Zucker rat," <i>J. Pharm. &amp; Exp. Ther.</i> , 1990, 253(1), 85-89	
	28	Thomas, J.B., et al., "N-substituted 9 $\beta$ -methyl-5-(3-hydroxyphenyl)morphans are opioid receptor pure antagonists," <i>J. Med. Chem.</i> , 1998, 41, 4143-4149	
	29	Werner, J.A., et al., "Synthesis of <i>trans</i> -3,4-dimethyl-4-(3-hydroxyphenyl)piperidine opioid antagonists: application of the <i>Cis</i> -thermal elimination of carbonates to alkaloid synthesis," <i>J. Org. Chem.</i> , 1996, 61(2), 587-597	
	30	Wittert, G., et al., "Tissue distribution of opioid receptor gene expression in the rat," <i>Biochem &amp; Biophys. Res. Commun.</i> , 1996, 218(3), 877-881	
	31	Zimmerman, D.J., et al., "Discovery of a potent, peripherally selective <i>trans</i> -3,4-dimethyl-4-(3-hydroxyphenyl) piperidine opioid antagonist for the treatment of gastrointestinal motility disorders," <i>J. Med. Chem.</i> , 1994, 37(15), 2262-2265	
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### U. S. PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Name	Class	Subclass
	32	4,176,186	11/27/79	Goldberg, et al.	424	260
	33	4,987,126	01/22/91	Bargiotti, et al.	514	34
	34	5,159,081	10/27/92	Cantrell, et al.	546	226
	35	5,250,542	10/05/93	Cantrell, et al.	514	315
	36	5,270,323	12/14/93	Milne, Jr., et al.	514	309
	37	5,434,171	07/18/95	Frank, et al.	514	331
	38	5,972,954	10/26/99	Foss, et al.	514	282

### FOREIGN PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Country	Translation	
					YES	NO
	39	WO 99/45925	09/16/99	PCT		

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